THE SCOTTISH OFFICE
Home and Health Department

Local Research Ethics Committees

LOCAL RESEARCH ETHICS COMMITTEES

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Chapter 1

INTRODUCTION

1.1 Health care and medical research is important, and the NHS has a key role in enabling it. The approval of research projects is an important management responsibility involving resourcing, financial implications and ethical issues. Such matters are generally best left to the local management team, but on ethical issues they need to take into account independent advice. The purpose of a local research ethics committee is to consider the ethics of proposed research projects, which will involve human subjects, and which will take place broadly within the NHS. The LREC's task is to advise the NHS body under the auspices of which the research is intended to take place. It is that NHS body which has the responsibility of deciding whether or not the project should go ahead, taking account of the advice of the LREC. For convenience, local research ethics committees are normally organised on a health board basis, but they exist to advise any NHS body. While a Committee of the Board they are not in any sense management arms of the Board.

1.2 The NHS bodies which will look to a LREC for advice on the ethics of proposed research projects are therefore:

- ❑ Health Boards, in respect of research taking place within their hospitals or community health services or by private sector providers under contract to the Health Board;
- ❑ Special Health Boards;
- ❑ NHS Trusts, in respect of research taking place within the units they control.

1.3 A LREC must be consulted about any research proposal involving:

- ❑ NHS patients, i.e. subjects recruited by virtue of their past or present treatment by the NHS, including those treated under contracts with private sector providers;
- ❑ fetal material and IVF involving NHS patients;
- ❑ the recently dead, in NHS premises;
- ❑ access to records of past or present NHS patients;
- ❑ the use of, or potential access to, NHS premises or facilities.

1.4 No NHS body should agree to such a research proposal which does not have the approval of the relevant LREC. No such proposal should proceed without the permission of the responsible NHS body. These requirements apply equally to researchers already working within the NHS and having clinical responsibility for the patients concerned, as they do to those who have no other association with the NHS and its patients, beyond the particular research project.

1.5 The relevant LREC in each case is normally that constituted in respect of the health board within the area of which the research is planned to take place. Special arrangements apply to multi-centre research, and these are referred to in Chapter 2 paragraph 18.

1.6 By agreement a LREC may also advise on the ethics of studies not involving NHS patients records or premises carried out for example by private sector companies, the Medical Research Council, or universities.

1.7 This Booklet gives guidance as follows:

- ❑ the establishment of LRECs and the administrative framework within which they work (Chapter 2);
- ❑ the ethical principles to which LRECs should have regard, and particular points that they should watch (Chapter 3);
- ❑ some special considerations concerning particular groups as research subjects (Chapter 4);
- ❑ the availability of further guidance (Chapter 5).

Chapter 2

THE ESTABLISHMENT AND OPERATION OF LRECS

Establishment

2.1 Although the LREC exists to provide independent advice to any NHS body within the geographical area of a health board, it will be the Health Board which takes responsibility for establishing the LREC, and for providing its administrative support. Each Health Board should consult any other NHS body which is likely to use the LREC before establishing it.

2.2 It does not follow, however, that the members of the LREC are in any way representative, nor beholden to any of the NHS bodies which collaborate in its establishment, nor that the LREC is an arm of the management of any of them. The object of consultation is to ensure that all the NHS bodies which will use the LREC should have confidence in its ability to provide sound research ethics advice.

2.3 In exceptional circumstances it may be appropriate to establish more than one LREC in a Health Board area. An example of this might be where there is a particularly high burden of work, perhaps originating from distinct research centres within the locality. In such a case the Health Board should secure agreement from all the relevant NHS bodies concerning the respective responsibilities of the LRECs, and should ensure that the administrative arrangements enable them to work together effectively.

Membership

2.4 A LREC should have 8 to 12 members. This should allow for a sufficiently broad range of experience and expertise, so that the scientific and medical aspects of a research proposal (see Chapter 3) can be reconciled with the welfare of research subjects, and broader ethical implications.

2.5 Members should be drawn from both sexes and from a wide age range. They should include:

- ❑ hospital medical and appropriate scientific staff
- ❑ nursing staff
- ❑ general practitioners
- ❑ 2 or more lay persons

2.6 Although drawn from groups identified with particular interests or responsibilities in connection with health issues, LREC members do not represent those groups. They are appointed in their own right, to participate in the work of the LREC as individuals of sound judgement and relevant experience.

2.7 The health professionals should include those occupied chiefly in active clinical care as well as those experienced in clinical investigation and research. As well as consulting the relevant NHS bodies, in connection with health professional appointments Health Boards should consult local professional

advisory committees and relevant health professional associations. Lay members should be appointed after consultation with the Local Health Council (LHC). At least one lay member should be unconnected professionally with health care and be neither an employee nor adviser of any NHS body.

Chairman and Vice-Chairman

2.8 After consultation with the relevant NHS bodies the Health Board should appoint a chairman and vice-chairman from amongst the members of the committee. At least one of these posts should be filled by a lay person.

Period of Appointment

2.9 Members should serve on LRECs for terms of 3 to 5 years. Terms of appointment may be renewed, but normally not more than 2 terms of office should be served consecutively.

Co-option

2.10 The LREC should, on its own initiative, seek the advice of specialist referees, or co-opt members to the committee, so as to cover any aspect, professional, scientific or ethical, of a research proposal which lies beyond the expertise of the existing members.

Legal Liability

2.11 LREC members may wonder whether they may be legally liable for injury caused to patients participating in research projects. Health Boards will wish to advise appointees on these matters. Legal advice available to the Scottish Office Home and Health Department is that there is little prospect of a successful claim against an LREC member for a mishap arising from research approved as ethical by the LREC. Any such claim would lie principally against the researcher concerned, and against the NHS body under the auspices of which the research took place. The principal defenders should seek to have any claim against an LREC member struck out. Those members of a LREC who are employees of a NHS body are already covered by NHS indemnity arrangements. The Health Board should also bear any costs in the case of other LREC members unless the member concerned is guilty of misconduct or gross lack of care in the performance of his or her duties and provided that if any claim is threatened or made, the member notifies the Health Board and assists it in all reasonable ways. If necessary the Health Board may give the following undertaking to this effect to LREC members who are not employees of a NHS body:

> "We confirm that the Health Board will take full responsibility for all your actions in the course of the proper performance of your duties as a member of the LREC other than those involving bad faith, wilful default or gross negligence; you should however notify the Health Board if any action or claim is threatened or made and in such event be ready to assist the board as required."

Health Boards should keep a record of which LREC members are covered by virtue of their NHS employment and which are not.

Working Procedures

2.12 The LREC should be geared to handling applications for ethical approval as quickly as possible and the Committee should always be able to demonstrate that

it has acted reasonably in reaching a particular decision. When research proposals are rejected by the LREC, the reasons for that decision should be made available to the applicant. Good standing orders and accurate record keeping are important. Standing orders should be drawn up by the Health Board, covering frequency of meetings and working methods. Conducting business by post or telephone should be discouraged and the situations in which Chairman's action can be taken should be clearly described.

Keeping a Register

2.13 The LREC should keep a register of all the proposals which come before it. The register should include the name and address of the organisation carrying out the research; names and qualifications of the research team; details of the premises in which the research will be conducted; medical support and other facilities available; a brief description of what is required of the research subjects and confirmation of compliance with any other guidelines (such as RCP or ABPI). This register would not normally be available for public consultation but should be open to the relevant NHS bodies.

Following Up

2.14 Once the LREC has approved the proposal, the researcher should be required to notify the committee, in advance, of any significant proposed deviation from the original protocol. Reports to the committee should also be required once the research is underway if there are any unusual or unexpected results which raise questions about the safety of the research. Reports on success, or difficulties, in recruiting subjects may also provide the LREC with useful feedback on perceptions of the acceptability of the project among patients and volunteers.

Confidentiality of Proceedings

2.15 As LREC members will not sit on the committee in a representative capacity they need to be able to discuss the proposals which come before them freely. For this reason LREC meetings will normally be private and the minutes taken will be confidential to the committee.

Producing an Annual Report

2.16 Each year the LREC should submit a report to the Health Board and copies should be sent to all the NHS bodies which the LREC exists to advise and to the LHC. The names of committee members, the number of meetings held and a list of proposals considered, including whether they were approved, approved after amendment, rejected or withdrawn should be included. This report should be available for public inspection.

Advice to non-NHS Bodies

2.17 Not all medical research involving human subjects takes place within the NHS. Even where there is **no** NHS involvement of any kind, the body conducting the research should be encouraged to submit its proposals to the LREC for advice. In such cases, the LREC should report to the Health Board the cost of its work so that that cost can be recovered from the outside body conducting the research. The LREC must also seek a full indemnity from the outside body against the possibility of future legal action.

Multicentre Research

2.18 Each LREC is free to arrive at its own decision when considering a proposal which is planned to take place in more than one area. It would, however, obviously be sensible – in the interests of eliminating unnecessary delay and of ensuring that similar criteria are used to consider a proposal – that committees should arrive at a voluntary arrangement under which one LREC is nominated to consider the issue on behalf of them all. Health Boards should positively encourage networks of neighbouring LRECs so that such co-operation is more easily achieved.

Chapter 3

CONSIDERATION OF RESEARCH PROPOSALS

The Application

3.1 To arrive at its decision on whether a research proposal is acceptable on ethical grounds the LREC will need to consider a great deal of information. The proposals which reach the LREC should be of a standard to enable the committee to discharge its functions without having to correct basic errors. Researchers and their supervisors are not absolved of responsibility for their work by the existence of the LREC.

3.2 The points to consider in any particular proposal will depend on the nature of the study. More detailed information is contained in the guidance which is available from various professional bodies (see Chapter 5). As a minimum, and there will be other points to consider, the LREC will need to know:

(i) Has the scientific merit of the proposal been or will be, properly assessed.
(ii) How will the health of the research subjects be affected.
(iii) Are there possible hazards and, if so, adequate facilities to deal with them.
(iv) What degree of discomfort or distress is foreseen.
(v) Is the investigation adequately supervised and is the supervisor responsible for the project adequately qualified and experienced.
(vi) What monetary or other inducements are being offered to the NHS body, doctors, researchers, subjects or anyone else involved.
(vii) Are there proper procedures for providing explanation and for obtaining consent from the subjects or where necessary their parents or guardians.
(viii) Has the appropriate information sheet for the subjects been prepared.

Type of Research Under Consideration

3.3 LRECs should consider the ethical implications of all research proposals which involve human subjects, including, for example, questionnaires. All proposals will belong to one of two categories, therapeutic or non-therapeutic research. Therapeutic research carries the prospect of direct benefit to the research subject. Non-therapeutic research, whilst designed to advance scientific knowledge and therefore be of collective benefit, is not expected to give a direct benefit to the research subject. Non-therapeutic research may involve "healthy" as well as "patient" volunteers.

3.4 Where people volunteer to take part in non-therapeutic research they should know that they cannot expect to derive any direct benefit from that participation. The LREC will therefore want to be satisfied that the risk to which they are submitting themselves can be justified by the expected collective benefit.

Recruitment

3.5 No-one should be made to participate in a research study against their will. Those recruiting participants should be careful to avoid exerting any undue

influence. This is especially important where the recruits are drawn from a subordinate or dependent group, e.g. employees, students, junior hospital staff. The researcher should emphasise that participation is entirely voluntary; that refusal will attract no sanction; that if they agree to participate they are free to leave the study at any time with no detriment to their standing or employment, and that they will not be required to give reasons for declining to participate or leaving the study. Patients who refuse to participate in research studies should be reassured that they are free to do so with no detriment to their treatment.

State of Health

3.6 The LREC should establish that the researcher accepts the responsibility of ascertaining that, on recruitment and during the study, volunteers do not have or acquire a health status contra-indicating the study. Volunteers for non-therapeutic research need not be in perfect health providing that their participation will not affect their underlying condition. Researchers should be satisfied about the state of health of such persons and a statement of any current medication being taken should be required from all recruited. Permission should be sought for notice to be sent when necessary to the volunteer's own General Practitioner about his or her participation in the study; and refusal by them to permit such communication should lead to their rejection as a participant.

Consent

3.7 The procedure for obtaining consent will vary according to the nature of each research proposal. The LREC will want to be satisfied on the level and amount of information to be given to a prospective subject. Some methods of study such as randomised controlled trials need to be explained to subjects with particular care to ensure that valid consent is obtained. The LREC will want to look at such proposals particularly carefully. They will also want to check that all subjects are told that they are free to withdraw without explanation or hindrance at any stage of the procedure and with no detriment to their treatment. An information sheet, to be kept by the subject, should be required in almost all cases.

3.8 Written consent should be required for all research, except where the most trivial of procedures is concerned. For therapeutic research consent should be recorded in the patient's medical records.

3.9 Some research proposals will draw their subjects from groups of people who may find it difficult or impossible to give their consent, for example the unconscious, the very elderly, the mentally disordered or some other vulnerable group. In considering these proposals the LREC should seek appropriate specialist advice and they will need to examine the proposal with particular care to satisfy themselves that proceeding without valid consent is ethically acceptable. (See Chapter 4)

3.10 SHHD issued with a letter to RHB Secretaries on 15 June 1971 a standard form for use in the generality of medical and dental procedures for which patient consent was required. Additional advice/guidance was issued in 1975 on the topic of parents refusal to consent to blood transfusions, emergency procedures and operations for their children (NHS Circular No 1975 (GEN)81) and in 1979 on consent to treatment for young people (SHHD/DS(79)2). The current procedures on consent are being reviewed and a new circular will shortly be issued.

Confidentiality

3.11 The LREC will need to be assured that all research will be conducted in accordance with current codes of practice and data protection legislation. Researchers should be asked to confirm that personal health information will be kept confidential, that data will be secure against unauthorised access and that no individual will be identifiable from published results, without his or her explicit consent. All data from which an individual is identifiable should be destroyed when no longer required for the purposes of the original research. If, exceptionally the researcher wishes to retain confidential information beyond the completion of the research, the LREC, the relevant NHS body and the research subject must first be made aware of the reasons for obtaining the information and the circumstances in which this might be disclosed. The subject's consent to these arrangements must be recorded.

3.12 Epidemiological research through studies of medical records can be extremely valuable. Patients are however entitled to regard their medical records as confidential to the NHS and should in principle be asked if they consent to their own records being released to research workers. However there will be occasions when a researcher would find it difficult or impossible to obtain such consent from every individual and the LREC will need to be satisfied that the value of such a project outweighs, in the public interest, the principle that individual consent should be obtained. Where a patient has previously indicated that he or she would **not** want their records released then this request should be respected.

3.13 Wherever possible consent should also be sought from the health professional responsible for the relevant aspect of the subject's care. Once information has been obtained from the records no approach should be made to the patient concerned without the agreement of the health professional currently responsible for their care.

3.14 Certain enquiries and surveys, involving only access to patient records, such as the post-marketing surveillance of drugs, which are in the public interest, do not need prior approval of an LREC. See Appendix A.

Financial Considerations

3.15 The LREC should examine any financial aspect of a research proposal which may influence the patient's judgement in consenting, or the researcher's judgement in his/her treatment of subjects, in such a way as to call the ethics of the research into question. Clearly any payments to subject or researcher must be considered, but it is also possible that benefits to an institution or department may raise similar ethical questions. Undue variations in payments between different sites in a multi-centre project may also raise questions. In general, however, the resource implications of a research project for the NHS body concerned are for consideration by the NHS management, not by the LREC.

3.16 Payment in cash or kind to volunteers should only be for expense, time, and inconvenience reasonably incurred. It should not be at a level of inducement which would encourage people to take part in studies against their better judgement, or which would encourage them to take part in multiple studies.

Compensation

3.17 Arrangements for compensation in the event of a research subject being harmed, whether by negligence or not, will vary according to what type of body is sponsoring the research proposal. The LREC should ensure that those who agree to participate in research, which may involve some risk, whether as patients or healthy volunteers, are told at the outset what arrangements will apply in their case. The LREC should seek evidence from the sponsor that these arrangements have adequate financial backing.

3.18 NHS bodies are not empowered to offer advance indemnity to participants in research projects. A person suffering injury as a result of having taken part in research would be able to pursue a claim for negligence through litigation. Each case would of course have to be considered on its merits.

3.19 Private sector companies sponsoring research are usually able to ensure that effective provision is made to compensate any research subject whose health may be affected. To this end LRECs should seek confirmation that any such company conducting or sponsoring a patient or healthy volunteer study accepts responsibility for compensation and provides details of the basis on which it will be provided, i.e. causation, fault, etc., plus evidence of their ability to fulfil it.

3.20 Volunteers must therefore be told in advance of all known risks and be made aware that there could also be unforeseen risks and of the possible difficulties in obtaining compensation.

Safety Requirements

3.21 Where a proposal involves the use of drugs, medicines, ionising radiation, appliances or medical devices, LRECs should:

- ❑ because of the relevance to safety, insist on assurances of the quality and stability of any substance to be administered. This may be done, for example, by requiring details of any relevant clinical trials exemption certificate or by requiring a certified statement that any investigations made at the pre-clinical stage of their development from which data have been submitted for consideration have been carried out to a standard no less than that required by the clinical trial exemption scheme operated by the Medicines Control Agency.
- ❑ for medical devices at pre-clinical stage not covered by the Medicines Act, require an assurance from the reseacher that the devices comply with appropriate safety standards and have been manufactured in accordance with Good Manufacturing Practice or under authenticated systems of quality assurance. Where applicable medical devices should conform to the Essential Requirements of the appropriate European Community Directive. The EC provisions will come into force over the next few years.
- ❑ require, in submissions involving complex data, a succinct statement and/or an expert summary.
- ❑ seek outside expert opinion if necessary, for example because there was no member of the ethics committee who could guide the committee on the particular field to be covered in the study.

LREC Advice not Requested or Ignored

3.22 If it comes to the attention of a committee that research is being carried out which it has not been asked to consider or which it has considered but its

recommendations have been ignored, then the LREC should bring the matter to the attention of its appointing authority, the relevant NHS body and to the appropriate professional body.

Declaration of Interest

3.23 Any member of the LREC who has an interest which may affect their consideration of a particular research proposal should be asked to declare that interest, and if necessary should temporarily withdraw from the committee.

Chapter 4

SPECIAL CONSIDERATIONS

Research on Children

4.1 Research proposals should only involve children where it is absolutely essential to do so and the information required cannot be obtained using adult subjects.

4.2 The Age of Legal Capacity (Scotland) Act 1991 provides that young people aged 16 and over have full capacity to consent to examination or treatment on their own behalf. A child under the age of 16 is also capable of giving valid legal consent to a medical procedure or treatment (including research) provided he or she is, in the opinion of the qualified medical practitioner attending him/her, capable of understanding the nature and possible consequences of the proposed procedure or treatment. The test is applicable whether the treatment concerned is directly for the child's benefit or not. In the case of non-therapeutic treatment it is advisable for the qualified medical practitioner to be satisfied that the child has a greater level of understanding than is necessary where the research is clearly therapeutic. However, the test remains the same and also applies whether or not the child is living with parents or guardians or independently.

4.3 It is generally beneficial for the parent(s) or guardian(s) of a child under the age of 16 to be informed, even where the child is capable of understanding the nature and possible consequences of the treatment or procedure. Informed parents or guardians are in a position to advise the child rather than take a decision for him/her or veto the child's decision. The medical practitioner should always seek to persuade such a child to involve a parent or guardian. However, if the child refuses to allow the parent(s) or guardian(s) to be informed the doctor should respect the rules of professional confidentiality. Persons or bodies other than parents or guardians may legally be in a position to give consent on behalf of a child to medical treatment. These include where a local authority has assumed parental rights in respect of a child under the Social Work Services Act 1968, or where a person has been awarded custody of a child by the Court.

4.4 Where the proposal is for non-therapeutic research all of the above applies but in addition the child must be subject to no more than minimal risk as a result of his/her participation.

4.5 The LREC should note that those acting for the child can only legally give their consent provided that the intervention is for the benefit of the child. If they are responsible for allowing the child to be subjected to any risk other than one so insignificant as to be negligible which is not for the benefit of that child, it could be said they were acting illegally. It should also be noted that the giving of consent by a parent or guardian cannot override the refusal of consent by a child who is competent to make that decision.

Research on Women

4.6 Where women are involved as research subjects the possibility of their being, or becoming, pregnant should always be considered. The recruitment of females of child-bearing age should always be justified by the researcher.

Research on Prisoners

4.7 Where the research subject is a prisoner the explicit consent of the Chief Executive of the Scottish Prison Service must be sought for the research proposal in addition to the consent of the subject.

Research on Mentally Disordered People

4.8 Research on mentally disordered people* requires particular care and sensitivity bearing in mind that they are vulnerable and some may not be able to give consent. There is a need to weigh the rights of an individual to consent or refuse to take part in research, and the particular status of those unable to consent against the need for research to advance the knowledge and treatment of mental disorders.

4.9 Consent must be freely given and based on information given in a form that is understandable to each individual. It is therefore necessary to take account of the capacity of the person to understand the information given and this in turn will depend on their intellectual state, mental disorder, and the possible variability of their mental state.

4.10 The presence of mental disorder does not by itself imply incapacity, nor does detention under the Mental Health (Scotland) Act 1984.

Proposals for Research

4.11 Proposals for research where capacity to consent is impaired will need particularly careful consideration by the LREC, with regard to the acceptability of the research in terms of the balance of benefits, discomforts and risks for the individual patient and the need to advance knowledge to the benefit of mentally impaired people in general. It is not appropriate to spell out the legal position in this document, consequently, as indicated in paragraph 3.9, specialist, and if necessary legal, advice should be taken when required. Members of LRECs and researchers should be aware of and draw on the Guidelines issued by the Royal Colleges, notably the Royal College of Psychiatrists and the Report of the Medical Research Council Working Party on the "Ethical Conduct Research on the Mentally Incapacitated" published in December 1991.

* Mental disorder means mental illness or mental handicap however caused or manifested.

Chapter 5

FURTHER READING

5.1 The current procedures on consent are being reviewed (see paragraph 3.10) and a new circular will be issued in the near future.

5.2 Guidelines on research ethics are also produced by various bodies within the UK. Among these are:

- The Medical Research Council
  20 Park Crescent
  LONDON
  W1N 4AL

- British Paediatric Association
  5 St Andrew's Place
  Regent Park
  LONDON
  NW1 4LB

- The Royal College of Psychiatrists
  17 Belgrave Square
  LONDON
  SW1X 8PG

- The Royal College of Physicians
  11 St Andrew's Place
  LONDON
  NW1 4L3

- The Association of the British Pharmaceutical Industry
  12 Whitehall
  LONDON SW1

- The Association of Independent Clinical Research Contractors
  Department of Toxicology and Therapeutics
  University of Wales College of Medicine
  Heath Park
  CARDIFF
  CF4 4XN

5.3 Finally, reproduced at Appendix A is a list of the kinds of survey which do not have to be referred to the LREC, and at Appendix B (and bearing original paragraph numberings) is an extract from *The Review of the Guidance on the Research Use of Fetuses and Fetal Material*, the "Polkinghorne Report". At Appendix C, by kind permission of the World Medical Association, is a reproduction of the Declaration of Helsinki.

APPENDIX A

EXAMPLES OF ENQUIRIES AND SURVEYS IN THE PUBLIC INTEREST WHERE NO REFERENCE TO AN LREC IS NECESSARY

The National UK Spontaneous Adverse Reaction Reporting Scheme (Yellow Card Scheme of CSM)

This is a scheme under which doctors, dentists and Procurator Fiscals use yellow card report forms voluntarily to report adverse drug reactions to the Committee on Safety of Medicines. (Pharmaceutical companies are obliged to make reports). It is a vital early warning mechanism for identifying adverse reactions not evident from clinical trials and enables CSM to monitor drug safety and keep prescribers informed.

Prescription Event Monitoring (PEM)

This is an established method of post marketing surveillance carried out by the Drug Safety Research Unit in Southampton. Patients treated with new medicines are identified from prescriptions and prescribers are contacted to provide information (on green forms). This is used to identify possible adverse drug reactions.

Company Sponsored Post Marketing Surveillance Studies (PMS)

The Committee on Safety of Medicines has recommended that pharmaceutical companies carry out PMS studies on new drugs intended for widespread long term use using cohorts of at least 10,000 patients. Guidelines on these studies were published in the British Medical Journal 1988; vol 296, pp 399–400. It is imperative that they include adequate numbers of patients to monitor drug safety and that their design and methods are appropriate for their stated scientific and medical objectives. Whether a project satisfies points 2, 4, 5, 13, 14, 17 and 18 of these guidelines should distinguish acceptable studies of this kind from any for promotional or "seeding" purposes.

APPENDIX B

CODE OF PRACTICE ON THE USE OF FETUSES AND FETAL MATERIAL IN RESEARCH AND TREATMENT

The guidance in this Chapter is taken from the Review of the Guidance on the Research Use of Fetuses and Fetal Material ("The Polkinghorne Report") CM 762, HMSO 1989 and the figures in brackets refer to the relevant paragraph in the text of the Report.

In this Code fetus means the embryo or fetus from implantation until gestation ends and, unless qualified by the words in utero, includes the fetus outside the womb. (1.3)

1. Treatment of the Fetus

1.1 Two categories of fetus are recognised:

(*a*) The live fetus, whether in utero or ex utero, which should be treated on principles broadly similar to those which apply to treatment and research conducted with children and adults. (2.4, 3.2)

(*b*) The dead fetus. The determination of death shall be by reference to the absence of vital functions, as indicated by the absence of spontaneous respiration and heartbeat after consideration of possibly reversible factors, such as the effects of hypothermia in the fetus, or of drugs or metabolic disorders in the mother. This determination shall be made or confirmed by a doctor responsible for the clinical management of the mother and the fetus and not involved with the subsequent unconnected use of fetal tissue. (3.7)

Only tissue from the dead fetus is ethically available for use in therapy.

1.2 It is unethical to administer drugs or carry out any procedures during pregnancy with the intent of ascertaining whether or not they might harm the fetus. (3.3)

1.3 In the case of nervous tissue only isolated neurones or fragments of tissue may be used for transplantation. (3.11)

2. Contents of the Uterus other than the Fetus

The contents of the uterus resulting from pregnancy other than the fetus (i.e. the placenta, fluid and membranes) may be used for research or therapeutic purposes subject to the conditions relating to screening at section 4.5 of this Code and those relating to finance at section 7(3.12).

3. Separation of the Supply of Fetal Tissue from the Practice of Research and Therapy

3.1 The decision to carry out an abortion must be reached without consideration of the benefits of subsequent use. The generation or termination of pregnancy to produce suitable material is unethical. (4.1)

3.2 The management of the pregnancy of any mother should not be influenced by use of the fetus in research or therapy. In this context, management of the pregnancy should be taken to include:

(*a*) the method and timing of an abortion;

(*b*) the clinical management of a mother whose fetus dies in utero or who has a spontaneous abortion.

3.3 No inducements, financial or otherwise, should be put to the mother or to those who are in a position to influence her decision to have her pregnancy terminated, or to allow fetal tissue to be used. (4.4)

3.4 The mother should not be informed of the specific use which may be made of fetal tissue, or whether it is to be used at all. (4.2, 4.6)

3.5 Those involved in the process of abortion and responsible for the clinical care of the mother should not knowingly be involved in research on the fetus or fetal tissue collected. Dissection of the dead fetus, research on it, or transplantation of fetal tissue should, when practicable, be on separate premises and certainly not in the same room. However, ethically acceptable exceptions to this degree of separation occur when research is concerned with the investigation of cases of fetal death in utero, or spontaneous abortion or analogous post-mortem concerns arising from previous medical history. (5.7)

3.6 The source must keep records indicating the next destination of any fetal tissue which is released for purposes of research or therapy, and it should have a means of satisfying itself that anyone to whom tissue is sent has satisfied the requirements of this Code. The mother's identity should not be revealed when fetal tissue is released, although some coding will be necessary which will enable her to be traced by those responsible for her clinical management, should relevant information come to light through examination of the fetal tissue. (5.3)

3.7 Any intermediary or tissue bank which receives or passes on fetal tissue must keep a record of the destination and origin of all tissue and not reveal details of the identity of the source to the user and vice versa. (5.4)

3.8 On the same principle the user should be able to satisfy itself that any material it receives has been procured in accordance with the requirements of this Code. It must keep records indicating the proximate source of any fetal tissue and the use to which it is put, but should not reveal details of the use to the source. (5.5)

3.9 Details about a fetus (e.g. gestational age) which might be of significance for research but could not be used for identification may be released by the source, but it is not acceptable for the source to be approached with requests for fetuses with particular characteristics. (5.6)

4. Consent

4.1 The written consent of the mother must be obtained before any research or therapy involving the fetus or fetal tissue takes place. Sufficient explanation should be offered to make the act of consent valid. (6.3)

4.2 Consent to the termination of pregnancy must be reached before consent is sought to the use of fetal tissue, and without reference to the possibility of that use. Provided the question of use is not introduced until consent to the termination of pregnancy has been obtained, it is permissible to deal with the 2 issues on the same occasion. (6.5)

4.3 It may be desirable to consult the father since, for example, tests on fetal tissue may reveal a finding of potential significance to him, and because he may have knowledge of a transmissible or hereditary disease, but his consent shall not be a requirement nor should he have the power to forbid research or therapy making use of fetal tissue. (6.7)

4.4 In the case of spontaneous abortions (or where death of the fetus has occurred in utero) consent to use fetal tissue should preferably be sought only after the fetus has died. (6.4)

4.5 Consent should be obtained from the mother to tests if any screening is to take place for transmissible disease or if any procedure is contemplated which could have similar consequences for the mother and affect her clinical management. Any such tests, and the counselling to accompany them, should be conducted according to the best current practice and guidance, in a manner which ensures that the principles of separation are maintained. (6.9)

5. Conscientious Objection

No member of the medical or nursing staff should be under any duty to participate in research or therapy involving the fetus or fetal tissue if he or she has conscientious objection. This right of non-participation does not extend to the prior or subsequent care of a patient thus treated. (2.11)

6. Ethics Committees

All research or therapy of an innovative character involving the fetus or fetal tissue should be described in a protocol and be examined by an ethics committee. Projects should be subject to review until the validity of the procedure has been recognised by the committee as part of routine medical practice. The ethics committee has a duty to examine the progress of the research or innovative therapy (e.g. by receiving reports). It should have access to records and be able to confirm that the material is in fact being used for the purpose set out in the protocol. It should also be able to examine the record of any financial transactions involving fetal tissue. Before permitting research the ethics committee must satisfy itself: (7.4)

(*a*) of the validity of the research or use proposed;

(*b*) that the objectives of the proposed use cannot be achieved in any other way;

(*c*) that the researchers or clinicians have the necessary facilities and skill.

7. Finance

There should be no monetary exchange for fetuses or fetal tissue. Profit from any dealing in fetal tissue or other contents of the uterus is unethical. (8.1, 8.3)

APPENDIX C

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Recommendations guiding physicians in biomedical research involving human subjects

Adopted by

THE 18th WORLD MEDICAL ASSEMBLY
Helsinki, Finland, June 1964

and amended by

THE 29th WORLD MEDICAL ASSEMBLY
Tokyo, Japan, October 1975

35th WORLD MEDICAL ASSEMBLY
Venice, Italy, October 1983

and the

41st WORLD MEDICAL ASSEMBLY
Hong Kong, September 1989

Introduction

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.

In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognised between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the result of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

I
Basic Principles

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.

3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.

8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the

study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subjects' freely-given informed consent, preferably in writing.

10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.

11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II
Medical Research Combined with Professional Care (Clinical Research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, re-establishing health or alleviating suffering.

2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

3. In any medical study, every patient – including those of a control group, if any – should be assured of the best proven diagnostic and therapeutic method.

4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.

5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (I,2).

6. The Physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III
Non-Therapeutic Biomedical Research involving Human Subjects (Non-clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.

2. The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.

3. The investigator or the investigating team should discontinue the research if in his/her or their judgement it may, if continued, be harmful to the individual.

4. In research on man, the interest of science and society should never take precedence over considerations related to the wellbeing of the subject.

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